REMARKS/ARGUMENTS

Claim Amendments

By the present amendment, claim 1 has been amended to remove the possibility that the sol-gel precursor is sodium silicate. Claim 4 has been amended so that it depends from claim 1. This latter amendment is a clarifying amendment which in no way alters the scope of claim 4.

The claim amendments have been made without prejudice and without acquiescing to any of the Examiner's objections. The Applicants submit that no new matter has been entered by the present amendment and entry of the amendments is respectfully requested.

The Official Action dated January 24, 2006 has been carefully considered. It is believed that the claims and figures submitted herewith and the following comments represent a complete response to the Examiner's comments and place the present application in condition for allowance. Reconsideration is respectfully requested.

Objections Withdrawn

The Applicants acknowledge and appreciate the Examiner's withdrawal of the objection to claims 5 and 15.

Claim Rejections Withdrawn

The Applicants acknowledge and appreciate the Examiner's withdrawal of all claim rejections as outlined on pages 3-5 of the Office Action.

New Claim Rejections

35 U.S.C. §102(b)

The Examiner has rejected claims 1-4, 11 and 14-19 under 35 U.S.C. §102(b) as being anticipated by Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421). The Applicants respectively traverse this rejection.

1. Summary of Gill

This publication is a general review article that summarizes the state of the art, in 2001, of sol-gel bioencapsulation. In his article Gill provides (1) an overview of the pertinent features of proteins (in consideration of bioencapsulation, pp 3405-3406); (2) an overview of the essentials of sol-gel nano-bioencapsulation (pp 3406-3408); (3) an overview of sol-gel precursors and matrixes that had been used for bioencapsulation to date (pp 3408-3410); an overview of what is known about bio-doped sol-gels (pp 3410-3411); (4) a summary of the reported applications for sol-gel bioencapsulates (pp 3411-3416): and (5) a summary of Gill's opinions regarding the problems facing the field of bioencapsulation and therefore the direction that research in this area should be going (pp 3416-3419). Gill therefore summarizes the myriad of options and combinations that have been and may be explored in the area of bioencapsulation. The teachings in Gill may be seen as a genus describing the many combinations of variables, as of 2001, that were available to a person skilled in the art when faced with the task of encapsulating a biomolecule in an inorganic matrix.

The Examiner contends that Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes comprising combining a liposome assembly, which includes the membrane-associated molecule, with a protein- and membrane-compatible sol-gel precursor under conditions to allow a gel to form wherein the sol-gel precursor is an organic polyol silane. The Applicants respectfully disagree.

2. Gill does not teach the use of an organic polyol silane as a sol-gel precursor

The Examiner contends that Gill teaches that, in a method of encapsulating biomolecules, in particular membrane associated molecules in a liposome assembly, the precursor to the sol-gel may be an organic polyol silane. The Examiner specifically refers to the section entitled *The Essentials of Sol-Gel Nano-bioencapsulation on* pp. 3406-3408 of Gill as well as Figure 1. On page 3406 of Gill, it is taught that the procedure for bioencapsulation involves (1) preparing an aqueous sol composed of a

partially or fully hydrolyzed alkoxysilane and (2) mixing the precursor sol with the biological. In one aspect Gill teaches that the precursor sol may be prepared as follows:

> Alkoxysilanes are 50-75% hydroly[zed] and transesterified with glycerol under acidic, basic, or alkoxide catalysts in alcohol solvent, to form water-soluble isolable poly(glyceryl silicates) and poly (glyceroxysiloxanes) which are dissolved in water.

Further, in Figure 1 it is taught, again, that simple alkoxysilanes are treated to form poly(glyceryl silicates), poly(glyceryl metallosilicates), poly(alkylglyceroxysilanes) or poly(oxometalloalkylglyceroxysilanes) which are dissolved in water to provide a "precursor gel solution" to which a biomolecule is added for entrapment. The Applicant submits that diglyceryl silane (DGS), related glycerylsilanes and other polyol-modified silanes, used in the methods claimed by the present Applicants are fundamentally different from the material(s) described in Gill. The poly(glyceryl silicates) described in Gill are prepared in a medium containing water, such as hydrochloric acid, particularly using acidic catalysts. Such conditions are ideal for alkoxysilane hydrolysis and, ultimately, condensation to prepare siloxane oligomers and polymers. It is not possible to prepare pure alkoxysilanes, such DGS and other polyol-modified silanes used in the methods claimed by the present Applicants, under these conditions (see C. J. Brinker and G. W. Scherer, Sol-Gel Science - The Physics and Chemistry of Sol-Gel Processing, New York, Academic Press, 1990 – p. 116 "Tetraalkoxysilanes, organotrialkoxysilanes, and diorganodialkoxysilanes hydrolyze upon exposure to water vapor"; "Hydrolysis is most rapid and complete when catalysts are employed."; "Many authors report that mineral acids are more effective catalysts…"). *At no point does Gill teach or suggest using an organic polyol silane (which, by definition, is not partially or fully-hydrolyzed) as the precursor for the entrapment of the biomolecule.*

3. Gill does not teach a method involving the specific combination of a liposome assembly comprising a membrane associated molecule with an organic polyol silane.

As stated above, Gill discloses a genus encompassing the many combinations of variables that are available to a person skilled in the art when faced with the task of encapsulating a biomolecule in an inorganic matrix. There is at no place in this publication that the specific combination of a liposome assembly, comprising a membrane-associated molecule and an organic polyol silane sol-gel precursor, is taught. Consideration of this issue will be the same as that for anticipation of a species covered by a generic chemical formula According to §2131.02 of MPEP:

> When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or delimited. If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. [Emphasis Added]

It is clear that, even if Gill did teach organic polyol silanes as precursors to sol-gels for use in bioencapsulation techniques, a person skilled in the art would not have been able to at once envisage the specific combination of a liposome assembly, comprising a membrane-associated molecule and an organic polyol silane sol-gel precursor, from the myriad of possible combinations. One need only to look at Figure 1 on page 3407 of Gill to see that there would be thousands of combinations of precursors, biomolecules, additives and mixing techniques and that it would be impossible for a person skilled in the art to at once envisage the combination that is claimed in the present invention.

It should be noted that at page 3418, 1st column, third paragraph, Gill teaches that substantial hurtles need to be overcome for the bioencapsulation of

> certain classes of biological, especially oligomeric biomolecules, membrane proteins, organelles and live cells. [Emphasis Added.]

Accordingly, this is further evidence that Gill does not teach a method involving the specific combination of a liposome assembly comprising a membrane-associated molecule and an organic polyol silane precursor since it is clear from his review of the art that the bioencapsulation of such molecules has not yet been successfully accomplished. This also further highlights the novelty and inventiveness of the present invention.

Since Gill does not teach (1) the use of an organic polyol silane as a precursor for any bioencapsulation, let alone the specific encapsulation of a liposome assembly, comprising a membrane-associated molecule; and (2) Gill does not describe the successful entrapment of any liposome assembly comprising a membrane-associated molecule, the Applicants submit that claim 1, and accordingly, claims 3-4, 11 and 14-19 which are all dependent on claim 1, are not anticipated by Gill. The Applicants note that claim 2 has been cancelled, rendering the Examiner's rejection of this claim moot.

In light of the above, the Applicants request that the Examiner's rejection of claims 1-4, 11 and 14-19 under 35 U.S.C. §102(b) be withdrawn.

35 U.S.C. §102(e)

The Examiner has rejected claims 1, 11 and 14 under 35 U.S.C. §102(e) as being anticipated by Robotti (U.S. PG Pub. No. 2003/0148291, filed February 5, 2002). The Examiner contends that Robotti teaches a method of immobilizing membrane-associated molecules in silica matrixes comprising combining a liposome-assembly, which includes the membrane associated molecule with a sol-gel precursor, wherein the sol-gel precursor is sodium silicate.

While not agreeing with the Examiner, to expedite the allowance of the claims in the present application, the Applicants have amended claim 1, and accordingly claims 11

and 14 dependent thereon, to remove the possibility that the sol-gel precursor is sodium silicate.

In light of the above amendment, the Applicants request that the Examiner's rejection of claims 1, 11 and 14 under 35 U.S.C. §102(e) be withdrawn.

35 U.S.C. § 103(a)

1. The Examiner has rejected claims 5, 6 and 8 under 35 U.S.C. § 103(a) as being obvious over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Montgomery (U.S. Patent No. 6,093,302, July 25, 2000). The Applicants respectfully traverse this objection.

Scope and Contents of Prior Art

Gill

As stated above, Gill is a general review article that summarizes the state of the art, in 2001, of sol-gel bioencapsulation. It provides a summary of what was known to date about the various biomolecules that have been entrapped in sol-gels, the various precursors used to prepare the sol-gels and the various reaction conditions.

Montgomery

Montgomery teaches a method of preparing polymers at a specific location on a substrate. The portions of the polymer are confined to certain areas on the substrate using electrochemical techniques. The Examiner contends that Montgomery teaches that, in a well-know polymerization method, the number of monomers can be varied from a number two or greater (column 16, lines 45-63). According to column 16, lines 45-48, of Montgomery, monomers include:

> all members of the set of small molecules that can be joined together to form a polymer.

Differences Between Prior Art and Claims At Issue

A. Gill

The Examiner contends that Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes, wherein the organic polyol silane precursor is poly(glyceryl silicate). First and foremost, and as explained above, the Applicants submit that a person skilled in the art would know that poly(glyceryl silicate) is not an organic polyol silane precursor. It is well known to those skilled in the art that silanes, by definition, are not the same chemical species as polysilicates. Polysilicates are prepared by the partial hydrolysis and condensation of orthosilicates and they have completely different reactivities compared to non-polymeric silanes, in particular under sol-gel forming conditions. For example, polysilicates, when used as precursors in the formation of sol-gels, are already well on the hydrolysis and condensation reaction pathway leading to sol-gels, and therefore tend to gel much more rapidly than the corresponding silanes. This allows less time for the manipulation of reaction conditions that are critical to control of the morphology and shrinkage characteristics of the resulting sol-gel.

Further as explained above, Gill does not even teach a method using the *specific combination* of poly(glyceryl silicate) and a liposome assembly comprising a membrane-associated molecule.

B. Montgomery

Montgomery teaches that in a polymerization reaction, the number of monomers can vary from at least 2 to greater. The Examiner contends that it would have been obvious to a person skilled in the art to include in the method of Gill, a method where the monomer number is two, as taught in Montgomery, to obtain di(glyceryl silicate), which is one of the precursor compounds claimed in claim 5 of the present application. The Examiner contends that, in light of Montgomery, it would take only routine skill to vary the number of monomers during a polymerization process, i.e. to vary the monomer number in the method described in Gill to arrive at the precursor polyol silanes used in the method of the present application.

The Applicant submits that argument proposed by the Examiner is incorrect. The "monomers" for silica are SiX_4 and H_20. Ultimately all four "X" groups will fall off and the crosslink density of a fully crosslinked material will be the same irrespective of the nature of X. Accordingly, if a polymerization reaction starts with $X_3Si\text{-}O\text{-}Si\text{-}X_3$ + water or SiX_4 + water, the same polymer product would result in both cases; i.e. there are no different monomers. Accordingly the difference between Gill and present invention is not a variation in monomer number and therefore Montgomery, in combination with GIll would not lead a person skilled in the art to the method as claimed in claim 5, or in claims 6 and 8 dependent thereon.

In light of the above, the Applicants request that the Examiner's rejection of claims 5, 6 and 8 under 35 U.S.C. § 103(a) be withdrawn.

2. The Examiner has rejected claim 7 under 35 U.S.C. § 103(a) as being obvious over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421). The Applicants respectfully traverse this objection.

Scope and Contents of Prior Art

Gill

As stated above, Gill is a general review article that summarizes the state of the art, in 2001, of sol-gel bioencapsulation. It provides a summary of what was known to date about the various biomolecules that have been entrapped in sol-gels, the various precursors used to prepare the sol-gels and the various reaction conditions. With respect to claim 7, the Examiner notes that Gill teaches a method of encapsulating bacteriorhodopsin using TMOS, which is not an organic polyol silane precursor. However, the Examiner alleges that it would have been obvious to a person skilled in the art include in the method of immobilizing a membrane associated molecule, such as bacteriorhodopsin, the use of an organic polyol silane precursor since such precursors are taught in Gill. The Examiner alleged that the person skilled in the art would do this

to use a photoactive protein, such as bacteriorhodopsin, as an optical device and transducer.

Differences Between Prior Art and Claims At Issue

As argued above, the Applicants submit that Gill does not teach or suggest an organic polyol silane precursor at all, for any use or application, accordingly, a person skilled in the art would not have been motivated by the teachings in Gill to encapsulate any biomolecule, let alone bacteriorhodopsin, using a method that includes such a precursor, such as claim 7. Further, the Applicants note that the encapsulation of bacteriorhodopsin reported in Gill did not involve the use of a liposome assembly. Accordingly, claim 7 is not obvious in light of Gill.

In light of the above, the Applicants request that the Examiner's rejection of claim 7 under 35 U.S.C. § 103(a) be withdrawn.

3. The Examiner has rejected claim 9 under 35 U.S.C. § 103(a) as being obvious over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001, hereinafter "Stowell"). The Applicants respectfully traverse this objection.

Scope and Contents of Prior Art

Gill

As stated above, Gill is a general review article that summarizes the state of the art, in 2001, of sol-gel bioencapsulation. It provides a summary of what was known to date about the various biomolecules that have been entrapped in sol-gels, the various precursors used to prepare the sol-gels and the various reaction conditions. As argued above, Gill does not teach the use of organic polyol silanes as precursors in methods to encapsulate biomolecules.

Stowell

Stowell teaches the use of silyl lipids as precursor molecules in the formation of bilayer or multilayer structures as well as in the formation of encapsulation material. Stowell teaches that lipid membranes and vesicles, including phospholipids vesicles, are fragile systems that require special conditions for encapsulation. Stowell does not teach the use of organic polyol silanes as precursors in methods to encapsulate lipid membranes and vesicles

Differences Between Prior Art and Claims At Issue

Since neither Gill nor Stowell teach or suggest an organic polyol silane precursor at all, for any use or application, a person skilled in the art would not have been motivated by the teachings in Gill and/or Stowell, to encapsulate any biomolecule, let liposomes comprising phospholipids, using a method that includes such a precursor, such as claim 9. Accordingly, claim 9 is not obvious in light of Gill in view of Stowell.

In light of the above, the Applicants request that the Examiner's rejection of claim 9 under 35 U.S.C. § 103(a) in view of Gill and Stowell be withdrawn.

4. The Examiner has rejected claim 9 under 35 U.S.C. § 103(a) as being obvious over Robotti (U.S. PG Pub. No. 2003/0148291, filed February 5, 2002) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001, hereinafter "Stowell").

Scope and Contents of Prior Art

Robotti

Robotti teaches a method of immobilizing biomolecules in silica matrixes comprising combining the biomolecule with a sol-gel precursor, wherein the sol-gel precursor is sodium silicate.

Stowell

Stowell teaches the use of silyl lipids as precursor molecules in the formation of bilayer or multilayer structures as well as in the formation of encapsulation material. Stowell

teaches that lipid membranes and vesicles, including phospholipids vesicles, are fragile systems that require special conditions for encapsulation.

The Examiner alleges that it would have been obvious to a person skilled in the art to include in the method of Robotti, a liposome assembly which includes a membrane associated molecule, wherein the liposome assembly comprises phospholipids as taught be Stowell.

While not agreeing with the Examiner, to expedite the allowance of the claims in the present application, the Applicants have amended claim 1, and accordingly claim 9 which is dependent thereon, to remove the possibility that the sol-gel precursor is sodium silicate which overcomes the Examiner's rejection.

In light of the above, the Applicants request that the Examiner's rejection of claim 9 under 35 U.S.C. § 103(a) in view of Robotti and Stowell be withdrawn.

5. The Examiner has rejected claim 10 under 35 U.S.C. § 103(a) as being obvious over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001, hereinafter "Stowell") as applied to claim 9 above, further in view of Dattagupta et al. (U.S. Patent No. 5,711,964, January 27, 1998, hereinafter "Dattagupta"). The Applicants respectfully traverse this objection.

For the reasons provided above, the Applicants submit that claim 9 is not obvious over the combination of Gill and Stowell. Claim 10, being dependent on claim 9 and merely adding the further limitation that the phospholipids comprises DOPC, would likewise be considered nonobvious over Gill and Stowell. Since Dattagupta only teaches that DOPC may be used to form a liposome vesicle, it goes no further to motivate a person skilled in the art to use an organic polyol silane precursor in a method for the encapsulation of liposome assemblies comprising membrane-associated molecules.

Accordingly, the Applicants submit that claim 10 is not obvious in view of Gill and Stowell, and further in view of Dattagupta.

In light of the above, the Applicants request that the Examiner's rejection of claim 10 under 35 U.S.C. § 103(a) in view of Gill and Stowell, and further in view of Dattagupta, be withdrawn.

6. The Examiner has rejected claim 10 under 35 U.S.C. § 103(a) as being obvious over Robotti (U.S. PG Pub. No. 2003/0148291, filed February 5, 2002) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001, hereinafter "Stowell") as applied to claim 9 above, further in view of Dattagupta et al. (U.S. Patent No. 5,711,964, January 27, 1998, hereinafter "Dattagupta").

Similar to the Applicants' response to the Examiner's objection to claim 9 in point 4 above, while not agreeing with the Examiner, to expedite the allowance of the claims in the present application, the Applicants have amended claim 1, and accordingly claim 10 which is dependent thereon, to remove the possibility that the sol-gel precursor is sodium silicate which overcomes the Examiner's rejection.

In light of the above, the Applicants request that the Examiner's rejection of claim 10 under 35 U.S.C. § 103(a) in view of Robotti and Stowell, and further in view of Dattagupta, be withdrawn.

7. The Examiner has rejected claims 12 and 13 under 35 U.S.C. § 103(a) as being obvious over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Lapidot et al. (U.S. PG Pub. No. US 2002/0064541 A1, published May 30, 2002, hereinafter "Lapidot") and Smith et al. (J. Am. Chem. Soc., Published on Web, March 28, 2002, Vol. 124, pp. 4247-4252, hereinafter "Smith").

The Examiner contends that it would have been obvious to a person skilled in the art to include in the method of Gill, the use of a humectant such as glycerol in a buffer solution

as taught by Smith to use during the drying process as taught by Lapidot to control the surface nature of the sol-gel matrix. As argued above, the Applicants submit that Gill does not teach or suggest the encapsulation of liposomes comprising a membrane-associate molecule in a sol-gel prepared from an organic polyol silane precursor. Accordingly, a person skilled in the art would not have been motivated to combine Gill with Lapidot and Smith to arrive at the invention as claimed in claims 12 and 13 of the present application and therefore, claims 12 and 13 are not obvious over these references.

In light of the above, the Applicants request that the Examiner's rejection of claims 12 and 13 under 35 U.S.C. § 103(a) in view of Gill in combination with Lapidot and Smith be withdrawn.

8. The Examiner has rejected claims 12 and 13 under 35 U.S.C. § 103(a) as being obvious over Robotti (U.S. PG Pub. No. 2003/0148291, filed February 5, 2002)) in view of Lapidot et al. (U.S. PG Pub. No. US 2002/0064541 A1, published May 30, 2002, hereinafter "Lapidot") and Smith et al. (J. Am. Chem. Soc., Published on Web, March 28, 2002, Vol. 124, pp. 4247-4252, hereinafter "Smith").

The Examiner alleges that it would have been obvious to a person skilled in the art to include in the method of Robotti, the use of a humectant such as glycerol in a buffer solution as taught by Smith to use during the drying process as taught by Lapidot to control the surface nature of the sol-gel matrix.

While not agreeing with the Examiner, to expedite the allowance of the claims in the present application, the Applicants have amended claim 1, and accordingly claims 12 and 13 which are dependent thereon, to remove the possibility that the sol-gel precursor is sodium silicate which overcomes the Examiner's rejection.
In light of the above, the Applicants request that the Examiner's rejection of claims 12 and 13 under 35 U.S.C. § 103(a) in view of Robotti in combination with Lapidot and Smith be withdrawn.

9. The Examiner has rejected claims 20 and 21 under 35 U.S.C. § 103(a) as being obvious over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Keeling-Tucker et al. (Chem. Mater., Published on Web, July 31, 2001, Vol. 13, pp. 3331-3350, hereinafter "Keeling-Tucker"). The Applicants respectfully traverse this rejection.

The Examiner contends that it would have been obvious to a person skilled in the art to include in the method of Gill, the use of the additive, PEO, as taught by Keeling-Tucker, to provide segregation into independent phases prior to gelation. As argued above, the Applicants submit that Gill does not teach or suggest the encapsulation of liposomes comprising a membrane-associate molecule in a sol-gel prepared from an organic polyol silane precursor. Accordingly, a person skilled in the art would not have been motivated to combine Gill with Keeling-Tucker to arrive at the invention as claimed in claims 20 and 21 of the present application and therefore, claims 20 and 21 are not obvious over these references.

In light of the above, the Applicants request that the Examiner's rejection of claims 20 and 21 under 35 U.S.C. § 103(a) in view of Gill in combination with Keeling-Tucker be withdrawn.

10. The Examiner has rejected claims 20 and 21 under 35 U.S.C. § 103(a) as being obvious over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Leung et al. (U.S. Patent No. 6,204,202, Issued March 20, 2001, hereinafter "Leung"). The Applicants respectfully traverse this rejection.

The Examiner contends that it would have been obvious to a person skilled in the art to include in the method of Gill, the use of an additive, such as a thermally degrading polymer, such as PEO, having a molecular weight ranging from about 200 to 2,000,000 Daltons as taught by Leung, to make silica nanoporous films (such as sol-gel) for sufficient mechanical strength that are also optimized to have a desirably low and stable

dielectric constant, without the need for further processing to make the film hydrophobic. As argued above, the Applicants submit that Gill does not teach or suggest the encapsulation of liposomes comprising a membrane-associate molecule in a sol-gel prepared from an organic polyol silane precursor. Accordingly, a person skilled in the art would not have been motivated to combine Gill with Leung to arrive at the invention as claimed in claims 20-23 of the present application and therefore, claims 20-23 are not obvious over these references.

In light of the above, the Applicants request that the Examiner's rejection of claims 20 - 23 under 35 U.S.C. § 103(a) in view of Gill in combination with Leung be withdrawn.

11. The Examiner has rejected claims 24 and 25 under 35 U.S.C. § 103(a) as being obvious over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Delamarche et al. (Langmuir, Published on the Web, September 11, 2003, Vol. 19, 8749-8758, hereinafter "Delamarche"). The Applicants respectfully traverse this rejection.

The Examiner contends that it would have been obvious to a person skilled in the art to include in the method of Gill, the use of an additive, such as the compound of Formula 5 in claim 25, as allegedly taught by Delamarche, to provide a simple and effective means to construct a stable hydrophilic structure. As argued above, the Applicants submit that Gill does not teach or suggest the encapsulation of liposomes comprising a membrane-associate molecule in a sol-gel prepared from an organic polyol silane precursor. Accordingly, a person skilled in the art would not have been motivated to combine Gill with Delamarche to arrive at the invention as claimed in claims 24 and 25 of the present application and therefore, claims 24 and 25 are not obvious over these references.
In light of the above, the Applicants request that the Examiner's rejection of claims 24 - 25 under 35 U.S.C. § 103(a) in view of Gill in combination with Delamarche be withdrawn.

Double Patenting

1. The Examiner has provisionally rejected claims 1 and 3-25 under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49 and 51 of co-pending Application No. 10/814,123 in view of Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421). The Applicants respectfully traverse this rejection.

The scope and content of Gill has been described in detail above.

The Examiner submits that Gill teaches a method of encapsulating proteins, which are part of assemblies such as bilayers, vesicles and membranes in order to preserve the gross structural integrity and large-scale internal mobilities of these structures. The Examiner specifically refers to p. 3406, first column, fifth paragraph of Gill in support of the Examiner's position. The Applicants submit that, while Gill may teach that it may be desirable to encapsulate proteins, which are part of assemblies such as bilayers, vesicles and membranes, in sol-gel materials, there is absolutely no evidence in Gill that this had actually been successfully done at the time that Gill was published. The information provided on p3406, first column, of Gill, merely lists the "critical aspects that need to be borne in mind when considering the sol-gel bioencapsulation of proteins". Further, on p. 3405, second column, there is merely a summary of "an overview of some pertinent features of proteins". Still further, there is no evidence in Table 4, on page 3415, of Gill that bacteriorhodopsin was part of a liposome assembly. Finally, It should be noted that at page 3418, first column, third paragraph, Gill teaches that substantial hurtles need to be overcome for the bioencapsulation of

> certain classes of biological, especially oligomeric biomolecules, membrane proteins, organelles and live cells. [Emphasis Added.]

Accordingly, Gill does not teach a method involving the specific combination of a liposome assembly comprising a membrane-associated molecule and an organic polyol silane precursor since it is clear from his review of the art, that the bioencapsulation of such molecules had not yet been successfully accomplished and Gill, as argued above,

does not teach the use of an organic polyol silane precursor. As stated above, this highlights the novelty and inventiveness of the present invention.

Since Gill does not teach that a liposome assembly comprising a membrane-associated molecule may be bioencapsulated in a sol-gel material, and in fact, this paper serves to highlight the difficulties associated with the bioencapsulation of such materials, the Applicants submit that a person skilled in the art would have no expectation of success and therefore no motivation to combine Gill with claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49 and 51 of co-pending Application No. 10/814,123, to arrive at the method claimed in claims 1 and 3-25 of the present application. Accordingly claims 1 and 3-25 are not obvious over claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49 and 51 of co-pending Application No. 10/814,123 in view of GIll.

In light of the above, the Applicants request that the Examiner's provisional rejection of claims 1 and 3-25 under the judicially created doctrine of obviousness-type double patenting over co-pending Application No. 10/814,123 in view of Gill be withdrawn.

2. The Examiner has provisionally rejected claims 1 and 3-25 under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-27 of co-pending Application No. 10/712,015 in view of Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421).

The Applicants would like to point out that co-pending Application No. 10/712,015 has been abandoned, thereby rendering the Examiner's provisional rejection moot.

In light of the above, the Applicants request that the Examiner's provisional rejection of claims 1 and 3-25 under the judicially created doctrine of obviousness-type double patenting over co-pending Application No. 10/712,015 in view of Gill be withdrawn.

Examiner's Response to Arguments

The Applicants note that all of the Examiner's arguments presented in paragraphs 35-41 of the Office Action are based on the Examiner's allegation that poly(glyceryl silicate) is an organic polyol silane. The Applicants submit that they have presented arguments above that clearly show that poly(glyceryl silicate) (PGS) is **not** an organic polyol silane. A person skilled in the art would know that silanes are not partially or fully hydrolysed or condensed materials, like PGS. The conditions described in Gill for the preparation of poly(glyceryl silicate) would not provide a silane. The advantages of using a silane as a precursor for the formation of sol-gel materials has only been recognized by the present Applicants, and include control over the kinetics of gelation which the present Applicants have found to provide greater control over the morphology and shrinkage characteristics of the resulting sol-gel. The Applicants would be very willing to discuss these issues in a telephone or in-person interview should the Examiner have further questions regarding the significant and fundamental differences between the polyol silanes of the present application and the polysilicates described in Gill.

Early and favorable action on the merits is awaited. Should the Examiner deem it beneficial to discuss the application in greater detail, the Examiner is invited to contact the undersigned by telephone at (416) 957-1683 at the Examiner's convenience.

Respectfully submitted,

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